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OBJECTIVES AND FOCUS OF THE THIRD SYMPOSIUM

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ORGANIZING COMMITTEE

Dear Colleague:

The National Institutes of Health is pleased to invite you to attend the third symposium on the Functional Genomics of Critical Illness and Injury, to be held April 21st and 22nd, 2005, at the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland.

The 2005 symposium will once again provide opportunities for communication among experts in the various disciplines of critical care medicine and the field of functional genomics. It will showcase the latest research findings, facilitate the exchange of information on state-of-the-art methodologies, and highlight the challenges we face now and in the future. Since the last meeting, in 2003, a great deal of important new data from patients and animal models has been analyzed; these data will be the focus of this year's meeting. With this information, clinicians and researchers are now poised to begin reaching consensus on how best to apply functional genomics to the study of critical illness and injury. This in turn will provide the groundwork for future collaborative interactions. To reflect these ends, the Organizing Committee has determined that the theme of this year's Symposium is "Identifying Research Priorities."

Topics of interest on the Program include genomic, transcriptomic, and metabolomic analysis; host-pathogen responses; and the ethical, legal, and societal implications of genomic research. Oral abstracts and poster sessions that allow one-on-one discussions between presenters and participants will be integrated into the program along with featured speakers. This more intimate setting will allow participants to gain deeper insights into topics and issues most relevant to their own work.

We will be accepting abstract submissions until March 1, 2005 (see our web site for details). At least eight of the abstracts accepted will be selected for oral presentation during the plenary sessions. The remainder will be presented at the poster sessions, providing an opportunity for informal discussion and the development of new collaborations.

This symposium is a unique opportunity for the exchange of ideas across the diverse fields committed to applying functional genomics and systems approaches to critically ill and injured patients. We look forward to welcoming you to Bethesda in April.

Sincerely,

Organizing Committee

J. Perren Cobb, MD Washington University in St. Louis

Anthony F. Suffredini, MD Clinical Center, NIH

Scott D. Somers, PhD National Institute of General Medical Sciences, NIH

Robert L. Danner, MD Clinical Center, NIH

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Dates

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Natcher Conference Center Bethesda, Maryland

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The conference fee for this event is \$125.

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Peter J. Munson, PhD Center for Information Technology, NIH BACKGROUND TO TH SYMPOSIA

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Septic shock, acute respiratory distress syndrome, acute renal and hepatic failure, myocardial dysfunction, coagulopathy, encephalopathy: these are some of the life-threatening responses to severe infection or traumatic injury facing patients and intensivists. Alone and cumulatively, each of these conditions increases the risk of death even after successful treatment of the underlying infection or injury. Mounting evidence points to the central role of the host's own inflammatory responses in the development of these syndromes. Yet despite substantial effort, treatment approaches directed at a single mediator or inflammatory pathway have had little success in altering outcomes of critically ill patients. It is clear that a more global understanding of complex biological systems is needed to advance care in this area and to reduce the currently substantial load of morbidity and mortality. Genomic technologies offer the potential to move in this direction.

Recent advances in computational biology and high-throughput technologies are enabling scientists to examine complex biological conditions in unprecedented detail, to view and interpret them at multiple levels, and thus have a better chance at capturing the interactive, emergent properties of adaptive and maladaptive host responses. In the specific case of critical illness, these technologies offer the potential to define maladaptive programs of gene expression induced by infection, trauma, or other inflammatory triggers and to detect biomarkers and genetic polymorphisms associated with these responses. These same tools also provide an important means to discover novel gene functions and relationships and to identify potential therapeutic targets.

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Genomic technologies are generating new resources and a tremendous wealth of data. Optimization of their use requires coordinated efforts on the part of many institutions to fashion the initial organizational framework. Four years ago, Drs. Perren Cobb, Robert Danner, and Anthony Suffredini formed the Consortium for Expression Profile Studies in Sepsis (CEPSIS) to address the needs of critical care investigators across 18 academic institutions interested in applying genomic technology to the study of critical illness and injury (http://www.cia.wustl.edu/cepsis%20redirect.htm). Four CEPSIS meetings took place, in Santa Fe, Boston, St. Louis, and Bethesda. The consortium then evolved into the Functional Genomics of Critical Illness and Injury Symposium, held in 2002 and 2003 at the National Institutes of Health. (A report of the 2003 meeting may be found in JAMA 2004; 291:287)

These symposia provide a unique venue for investigators to discuss the opportunities and challenges of genomic technologies in the care of critically ill and injured patients. The symposium series has attracted generous funding by the NIH Clinical Center, NIGMS, NHGRI, NCI, NIAMS, NICHD, NIAID, and Office of Rare Diseases (Office of the Director), as well as the interest of several hundred investigators from more than 10 countries who attended the meetings in 2002 and 2003.

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The goal of the Functional Genomics of Critical Illness and Injury Symposia is to bring together those with the diverse skills sets necessary to apply genomics and systems analysis to the study of critical illness and injury. The objectives are three-fold: education, consensus, and collaboration. Thus, our success will be measured in the tangible deliverables that address these objectives. The previous two Symposia provided an educational forum for those interested in new high-throughput technology and systems approaches to analysis. Since our last meeting over a year ago, a critical mass of important new data from patients and animal models have been analyzed, the focus of this year's Symposium. Thus, we are now poised to begin reaching consensus on how best to apply functional genomics to the study of critical illness and injury. This in turn will provide the groundwork for future collaborative interactions. To these ends, the Organizing Committee is pleased to announce that the theme of the 3rd annual Symposium is "Identifying Research Priorities".

In 2005 our primary focus will be on the rapidly evolving technologies of genomic, transcriptomic, proteomic, and metabolomic analysis. This educational focus will be particularly important as the cost of the technology decreases and tools move from the hands of investigators in large-scale collaborative projects to those who work in independent centers or laboratories. As in the past, featured speakers will lend their expertise in related fields such as cancer research to demonstrate the power of genomic and related technologies and their optimal use. Plenary speakers will discuss the application of functional genomics to patients with critical illness or injury with particular reference to host-pathogen interactions, an underappreciated and understudied influence on the outcomes of these patients. The 2005 program will also emphasize the increasing involvement of leaders in computational biology, biostatistics, and systems engineering. Highlighting the program will be a discussion of the ethical, legal, and societal consequences of the knowledge gained from these investigations, particularly as they affect the design of clinical trials, issues of informed consent, and the health and behavior of subjects/patients and their right to privacy.

We welcome your participation and look forward to a stimulating and productive symposium.

Selected Speakers and Topics

. Genomics: SNPs and Outcome

Lisa D. Brooks, PhD, on the HapMap Project Stephen J. Chanock, MD, on molecular epidemiology Jean-Paul Mira, MD, PhD, on sepsis polymorphisms, Part I Frank Stüber, MD, on sepsis polymorphisms, Part II

The Human Proteome Project

Samir M. Hanash, MD, PhD

Transcriptomics: Biomarkers and Targets

Trinad Chakraborty, PhD, on the German National Genome Research Network Hector R. Wong, MD, on the applications of functional genomics to pediatric critical care Lyle L. "Linc"Moldawer, PhD, on inflammation and host response

• Ethical, Legal, and Societal Implications

Jeffrey R. Botkin, MD, MPH, on genetic exceptionalism Timothy Buchman, PhD, MD, on ethical, legal and social implications in the ICU

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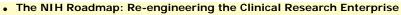
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Robert A. Star, MD

• Proteomic, Metabolomic, and Organ Responses

Patricia Molina, MD, PhD, on allostasis and the host response
David G. Camp, PhD, on plasma proteome and the host response to inflammation
Adam Seiver, MD, PhD, on organ complexity: modeling controller dysfunction
Gerald Saidel, PhD, on dynamic systems modeling of cellular metabolic processes with organ and whole-body responses

We welcome your participation and look forward to a stimulating and productive symposium.



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Symposium Sponsors The National Institute of General Medical Sciences Critical Care Medicine Department, Warren Grant Magnuson Clinical Center Office of Rare Diseases, Office of the Director SPONSORS ORGANIZING COMMITTEE National Human Genome Research Institute National Cancer Institute Microarray User Group **Proteomics Interest Group** The following Organizations have endorsed this conference: American Association for the Surgery of Trauma

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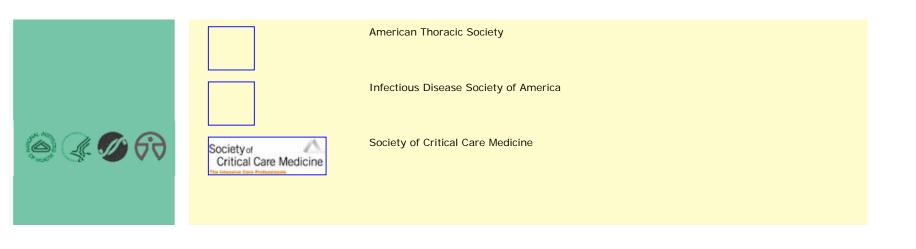
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THURDAY, APRIL 21, 2005

FRIDAY APRIL 22 2005

8:00 am Introduction

J. Perren Cobb, MD

Washington University, St. Louis

8:15 am Welcoming Remarks

Jeremy M. Berg, PhD

National Institute of General Medical Sciences, NIH

Featured Speaker

8:30 am The HapMap Project

Lisa D. Brooks, PhD

National Human Genome Research Institute, NIH

Plenary Session

Genomics: SNP's and Outcome

9:00 am	Molecular Epidemiology Stephen J. Chanock, MD National Cancer Institute, NIH

9:20 am **Polymorphisms of PRR and Severe Sepsis**

Jean-Paul Mira, MD, PhD

Cochin-St. Vincent de Paul University Hospital, Paris,

France

9:40 am Sepsis Polymorphisms: Germany

Frank Stüber, MD

Friedrich-Wilhelm University, Bonn, Germany

10:00 am Panel Discussion

Lisa D. Brooks, PhD

Stephen J. Chanock, MD Jean-Paul Mira, MD, PhD

Frank Stüber, MD

10:30 am Poster Session/Exhibit Viewing

Refreshments in Exhibit Hall

Featured Speaker

11:30 am Proteomic Global Profiling for Cancer

Biomarker Discovery Samir M. Hanash, MD, PhD

Fred Hutchinson Cancer Research Center

Noon	Lunch/Exhibit Viewing	
1:00 pm	Oral Poster Presentations	
2:00 pm	Poster Session/Exhibit Viewing Refreshments in Exhibit Hall	
Plenary Session Transcriptomics: Biomarkers and Targets		
2:30 pm	Gene Expression Signatures in Injury and Sepsis Trinad Chakraborty, PhD Justus-Liebig University, Giessen, Germany	
2:50 pm	Microarray Analyses in Pediatric Septic Shock Hector R. Wong, MD Cincinnati Children's Hospital Medical Center	
3:10 pm	Inflammation and Host Response Lyle L. "Linc" Moldawer, PhD University of Florida College of Medicine	
3:30 pm	Panel Discussion Trinad Chakraborty, PhD Hector R. Wong, MD Lyle L. "Linc" Moldawer, PhD	



3:50 pm	Poster Session Reception
4:30 pm	Poster Session Concludes
All day	Exhibits Open

THURDAY, APRIL 21, 200

FRIDAY, APRIL 22, 2005

8:15 am Welcoming Remarks

Anthony Suffredini, MD Clinical Center, NIH

Featured Speaker

8:30 am Genetic Determinism and Genetic Exceptionalism

Jeffrey R. Botkin, MD, MPH

University of Utah

Plenary Session Ethical, Legal, and Societal Implications

9:00 am The Ethical, Legal, and Societal Implications of Genomic Research of

Complex Traits Vivian Ota Wang, PhD

vivian Ota Wang, PhD

National Human Genome Research Institute, NIH

9:30 am Ethical, Legal, and Social Implications in the ICU

Timothy G. Buchman, PhD, MD Washington University in St. Louis

9:50 am Panel Discussion

Jeffrey R. Botkin, MD, MPH Vivian Ota Wang, PhD

Timothy G. Buchman, PhD, MD

10: 20 am Poster Session

Refreshments

11:00 am	Oral Poster Presentations	
Noon	Lunch	
Featured Speaker		
1:00 pm	The NIH Roadmap: Re-engineering the Clinical Research Enterprise Robert A. Star, MD National Institute of Diabetes and Digestive and Kidney Diseases, NIH	
Plenary Session Proteomic, Metabolomic, and Organ Responses		
1:30 pm	Neurobiology of the Stress Response; Neuroendocrine-Immune Interactions Patricia Molina, MD, PhD Louisiana State University Health Sciences Center	
1:50 pm	The Plasma Proteome and the Host Response to Inflammation David G. Camp, PhD Pacific Northwest National Laboratory, DOE	
2:10 pm	Cardiac Output Variations: Modeling Controller Dysfunction Adam Seiver, MD, PhD Respironics, Inc., Sacramento, CA	
2:30 pm	Break with refreshments	
2:50 pm	Dynamic Systems Modeling of Cellular Metabolic Processes with Organ and Whole-Body Responses Gerald M. Saidel, PhD Case Western Reserve University	
3:10 pm	Panel Discussion Patricia Molina, MD, PhD David G. Camp, PhD Adam Seiver, MD, PhD Gerald M. Saidel, PhD	



3:40 pm Closing Remarks

4:20 pm Adjourn

LISA D. BROOKS, PH [

TIMOTHY G. BUCHMAN PH D, MD

DAVID G. CAMP, PH D

TRINAD CHAKRABORTY, PHIL

STEPHEN J. CHANOCK, MC

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Jeremy M. Berg, PhD
Director
National Institute of General Medical Sciences
National Institutes of Health
Bethesda, Maryland

Speaker Topic: Welcoming Remarks

Dr. Berg became director of the National Institute of General Medical Sciences (NIGMS) in November 2003. He oversees a \$1.9 billion budget that funds basic research in the areas of cell biology, biophysics, genetics, developmental biology, pharmacology, physiology, biological chemistry, bioinformatics, and computational biology. The Institute supports more than 4,500 research grants-about 10 percent of the grants funded by NIH as a whole-as well as a substantial amount of research training and programs designed to increase the number of minority biomedical scientists.

Prior to his appointment as NIGMS director, Dr. Berg directed the Institute for Basic Biomedical Sciences at The Johns Hopkins University School of Medicine in Baltimore, MD, where he also served as professor and director of the Department of Biophysics and Biophysical Chemistry. In addition, he directed the Markey Center for Macromolecular Structure and Function and co-directed the W.M. Keck Center for the Rational Design of Biologically Active Molecules at the university.

Dr. Berg's research focuses on the structural and functional roles that metal ions, especially zinc, have in proteins. He has made major contributions to understanding how zinc-containing proteins bind to DNA or RNA and regulate gene activity. His work, and that of others in the field, has led to the design of metal-containing proteins that control the activity of specific genes. These tailored proteins are valuable tools for basic research on gene function and could one day have medical applications in regulating genes involved in diseases as well. Dr. Berg has also made contributions to our understanding of systems that target proteins to specific compartments within cells and to the use of sequence databases for predicting aspects of protein structure and function.

Dr. Berg served on the faculty at Johns Hopkins from 1986-2003. Immediately before his faculty appointment, he was a postdoctoral fellow in biophysics at the university. His honors include a Presidential Young Investigator Award (1988 -1993), the American Chemical Society Award in Pure Chemistry (1993), the Eli Lilly Award for Fundamental Research in Biological Chemistry (1995), and the Maryland Outstanding Young Scientist of the Year (1995). He also received teaching awards from both medical students and graduate students and served as an advisor to the Johns Hopkins Postdoctoral Association from its founding.

Dr. Berg received B.S. and M.S. degrees in chemistry from Stanford University in 1980 and a Ph.D. in chemistry from Harvard University in 1985. He is a coauthor of more than 120 research papers and three textbooks, *Principles of Bioinorganic Chemistry*, *Biochemistry* (5th Edition), and *A Clinical Companion to Accompany Biochemistry*.

NIGMS supported Dr. Berg's research from 1986-2003.



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Jeffrey R. Botkin, MD, MPH

Professor, Department of Pediatrics; Adjunct Professor of Human Genetics Adjunct Professor, Department of Internal Medicine - Division of Medical Ethics University of Utah School of Medicine Salt Lake City, Utah

Speaker Topic: Genetic Determinism and Genetic Exceptionalism

Dr. Botkin is the Associate Vice President for Research Integrity at the University of Utah. He was an undergraduate at Princeton University and received his M.D. from the University of Pittsburgh and an MPH from Johns Hopkins University. Dr. Botkin was also a fellow in Law, Ethics, and Health at Johns Hopkins in affiliation with the Kennedy Institute of Ethics at Georgetown. He has over 20 years' experience in the clinical care of pediatric patients. His research is focused on the ethical, legal, and social implications of genetic technology, with a particular emphasis on research ethics, genetic testing for cancer susceptibility, newborn screening, and prenatal diagnosis. Dr. Botkin currently is Chair of the Committee on Bioethics for the American Academy of Pediatrics and co-Chair of the Ethics Working Group of the National Children's Study. He is a fellow of the Hastings Center and serves on a number of federal, local, and national advisory boards. His publications include: Genetics and Criminality: The Potential Misuse of Scientific Information in Court and Access to the Genome: The Challenge to Equality.



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Lisa D. Brooks, PhD
Program Director
Genetic Variation Program
National Human Genome Research Institute
National Institutes of Health
Bethesda, Maryland

Speaker Topic: The HapMap Project

Dr. Brooks became the Program Director of the NIH Genetic Variation Program at the National Human Genome Research Institute in 1997. Prior to this appointment she was a Research Assistant in the Biology Departments at the University of California, San Diego, and Stanford University. She was then a Research Associate in the Statistics Department at North Carolina State University. From 1987-1994 Dr. Brooks was an Assistant Professor of Biology and Medicine in the Ecology and Evolutionary Biology Department at Brown University. From 1994 -1997 she was the Program Officer in the Division of Environmental Biology in the Population Biology Program at the National Science Foundation.

Recipient of the NIH Director's Award for the HapMap Project (2003) and the NHGRI Awards of Merit for the HapMap Project and the CEGS Program (2002, 2003), Dr. Brooks has written three requests for applications at NHGRI.

Dr. Brooks received her B.S. in Biology from Stanford University and her Ph.D. in Biology from Harvard University.



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Timothy G. Buchman, PhD, MD, FACS, FCCM

Harry Edison Professor, Surgery Division of General Surgery Chief; Burn, Trauma, Surgical Critical Care Section Washington University School of Medicine in St. Louis St. Louis, Missouri

Speaker Topic: Genetic Testing in the Acute Care Environment: Ethical, Legal and Social Aspects

In addition to the positions mentioned above, Dr. Buchman is Professor of Anesthesiology and of Medicine at Washington University School of Medicine in St. Louis. He is also Director of the Level I Trauma Center, co-Director of the Surgery/Burn/Trauma ICU, and Attending Surgeon at Barnes Jewish Hospital in St. Louis.

Prior to moving to St. Louis, Dr. Buchman was Associate Professor of Surgery, Assistant Professor of Emergency Medicine, and Director of the Training Program in Surgical Critical Care at The Johns Hopkins University School of Medicine, where he also held a joint appointment in Molecular Biology and Genetics.

The Associate Editor of *Shock*, Dr. Buchman has also been a member of the following editorial boards: *Critical Care Medicine*, *International Journal of Surgical Investigation*, *The Journal of Surgical Research*, and *The Journal of the American College of Surgeons*. He has published approximately 150 journal articles, abstracts, books, and chapters. Currently Dr. Buchman has three National Institutes of Health grants.

An active member of the Society of Critical Care Medicine, Dr. Buchman is the immediate Past President as well as a member of the Strategic Planning Committee. Previously he chaired the following SCCM organizational bodies: Research Division, Project IMPACT Advisory Committee, and the Undergraduate Education Subcommittee of the Educational Affairs Division. He has served the American College of Surgeons as a member of the Surgical Research and Education Committee and Course Director for the Young Surgical Investigators' Conference.

Additionally, Dr. Buchman is a member of the following professional societies: American Association for the Surgery of Trauma, American Surgical Association, Association for Academic Surgery, Eastern Association for the Surgery of Trauma, Shock Society, Society of University Surgeons, and Surgical Infection Society.

Washington University has honored Dr. Buchman with the Senior Class Award for Teacher of the Year and the Evarts A. Graham Resident Teaching Award. He is the recipient of the Dr. Harold Lamport Research Award Citation and the First Prize Resident's Award from Contemporary Surgery. While at Hopkins, Dr. Buchman was presented with the Anthony L. Imbembo Teaching Award and the Baltimore Academy Teaching Award. He received the John Van Prohaska Award and the Merck Award from the University of Chicago.

Dr. Buchman completed his fellowship in Traumatology and Critical Care at the Maryland Institute for Emergency Medical Service Systems and his residency and internship at The Johns Hopkins Hospital in Baltimore. He received a medical degree, a doctorate in virology, a master's degree in organic chemistry, and a bachelor's degree in chemistry from the University of





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David G. Camp II, PhD

Associate Director

Proteomics Research Resource for Integrative Biology for the National Center for Research Resources Richland, Washington

Speaker Topic: The Plasma Proteome and the Host Response to Inflammation

Dr. Camp's work focuses on developing automated methods for sample processing of cells, proteins, and peptides in combination with the introduction of stable isotope labels for quantitative measurements of proteome samples from two or more different sample conditions. Current projects include working with medically important microbes and viruses, mapping transient events in signal transduction pathways, characterizing the proteomes of mammalian cells and tissues, and identification and quantification of proteins in human blood plasma.

From 1989 to 1999 Dr. Camp was a tenured faculty member in the Chemistry Department at Eastern Oregon University in La Grande. During that time, he served in several faculty/student research appointments at Pacific Northwest National laboratory (PNNL) and was selected as a PNNL affiliate staff scientist in 1994. Dr. Camp joined PNNL as a senior research scientist in 2001, following one year in the private sector.

Dr. Camp received his B.S. in Chemistry from Albertson's College of Idaho and his Ph.D. from the University of Montana. He completed his post-doctorate work at the University of Houston and at PNNL. He was awarded the Summer Merit Award/ Research Grants at Eastern Oregon University in 1992, 1994, 1995, 1996, 1998, and 1999 and was Chair of the American Chemical Society, Richland Section, in 1992 and past-Chair in 1993.



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Trinad Chakraborty, PhD

Professor of Microbiology Director of the Institute of Medical Microbiology University Teaching Hospital of Giessen Giessen, Germany

Speaker Topic: Genome-Wide Molecular Signatures in Sepsis

Dr. Chakraborty obtained his B.Sc. with honors from the University College, London, and his Ph.D. summa cum laude from the Free University of Berlin, Germany. He received his Habilitation from the University of Wuerzburg and was Heisenberg Scholar of the German Research Foundation (DFG). Currently, Dr. Chakraborty is Professor and Director of the Institute of Medical Microbiology of Justus-Liebig-University, Giessen, Germany. He is also chairman and coordinator of both the Infection and Inflammation Network of the German National Genome Research Network (NGFN) and the Giessen Research Center in Infectious Diseases (GRID) and is an Executive Member of the Steering Committee of the NGFN. Dr. Chakraborty is also Vice-Chairman of the Collaborative Research Initiative (Sonderforschungsbereich SFB 535) on "Adhesion, Invasion and Intracellular Lifestyles of Pathogens" funded by the German Research Foundation (DFG). He is co-Founder and Chief Scientific Advisor to the company TGC Biomics in Mainz, Germany, which has specialist proprietary technologies in the area of pharmaceutical proteins, pharmaccines, and protein and gene delivery systems.

Dr. Chakraborty's areas of scientific interest are functional genomics of host-pathogen interactions, gene targeting, and genomics of critical illness and sepsis. He served on the editorial boards of several professional journals and is ad-hoc reviewer for numerous scientific journals.

Dr. Chakraborty is recipient of a number of Personal (peer-reviewed) Research Grants from the German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), German Cancer Research Council, Humboldt Foundation, World Health Organisation, and European Union. He is the author and co-author of over 180 publications in peer-reviewed journals.

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ADAM SEIVER, MD, PH D

ROBERT A. STAR, MD

VIVIAN OTA WANG, PH D

HECTOR R. WONG, MD

Stephen J. Chanock, MD

Principal Investigator Advanced Technology Center National Cancer Institute National Institutes of Health Bethesda, Maryland

Speaker Topic: Molecular Epidemiology

Dr. Chanock's laboratory is located at the Advanced Technology Center, where he is the Director of the Core Genotyping Facility of the Intramural Program of the NCI. Dr. Chanock is also co-Chair of the faculty of Genetics, Genomics, and Proteomics in the NCI. His work focuses on mapping the genetic contribution of complex diseases, such as cancer, and he has a strong interest in dissecting the genetic basis of outcomes in cancer, specifically infections complications.

Dr. Chanock received his A.B. from Princeton University and his M.D. from Harvard Medical School. He completed training in pediatrics, pediatric infectious diseases, and pediatric hematology/oncology at Boston Children's Hospital and the Dana-Farber Cancer Institute. Dr. Chanock is certified by the American Board of Pediatrics and a Diplomate of the Subsection Pediatric Hematology/Oncology and the Subsection Pediatric Infectious Diseases. He is a member of numerous professional organizations and is on the editorial board of *Genes and Immunity* and *Human Mutation*. Dr. Chanock has authored more than 120 peer-reviewed publications.

JEFFREY R. BOTKIN, MD, MPH

LISA D. BROOKS, PH D

PH D, MD

DAVID G. CAMP, PH I

TRINAD CHAKRABORTY, PH [

STEPHEN J. CHANOCK, ME

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HECTOR R. WONG, MI

Samir M. Hanash, MD, PhD

Full Member Fred Hutchinson Cancer Research Center Seattle, Washington

Speaker Topic: Proteomic Global Profiling for Cancer Biomarker Discovery

Dr. Hanash's interests and expertise focus on the development and application of integrated approaches to the molecular profiling of cancer, with particular emphasis on proteomics. Dr. Hanash's Ph.D. training is in human genetics and his clinical training in pediatric oncology. He was a program principal investigator (PI) for multi-investigator projects funded by the National Cancer Institute (NCI) while at the University of Michigan, including program projects. Most recently he has been the PI for an NCI-funded Director's Challenge program, which focuses on molecular profiling of lung, colon, and ovarian cancer; and PI of an NCI-funded Cancer Biomarker Development program, which focuses on the application of proteomics to the discovery of protein markers for the early diagnosis of lung and GI cancers. Dr. Hanash has organized and participated in several workshops sponsored by the NCI on cancer diagnostics and molecular profiling. He recently relocated from the University of Michigan to the Fred Hutchinson Cancer Research Center to lead a newly developed program in Molecular Diagnostics. Dr. Hanash will serve as program director for this project.



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HECTOR R. WONG, ME

Jean-Paul Mira, MD, PhD

Professor of Medical Intensive Care Cochin-St.Vincent de Paul University Hospital Medical Intensive Care Unit Paris, France

Speaker Topic: Pathogen Recognition Receptors Polymorphism

Dr. Mira received his M.D. from Reims Medical School in France, his Master's of Molecular and Cellular Biology from University of Paris V, and his Ph.D. from the University of Paris VI. In 2000 he became head of a research group on innate immunity and genetic predisposition to critical illness and received the Award of the French Society of Critical Care for the best publication of the year.

Dr. Mira has been a member of the French Society of Critical Care since 1990, President of the Scientific Committee of the French Society of Critical Care since 2002, and a member of the European Society of Intensive Care since 1999. He serves as a regular reviewer for the following journals: *Critical Care Medicine, American Journal of Respiratory Diseases, Shock,* and *Cytokine Network*. He is widely published in France and internationally, and has written thirteen chapters and several books.

JEFFREY R. BOTKIN, MD, MPH

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ROBERT A. STAR, ME

VIVIAN OTA WANG, PHIC

HECTOR R. WONG, MC

Lyle L. Moldawer, PhD

Professor of Surgery Vice Chairman for Research University of Florida College of Medicine Gainesville, Florida

Speaker Topic: Inflammation and Host Response

Dr. Moldawer joined the Department of Surgery, University of Florida College of Medicine faculty in September, 1993, after spending seven years on the faculty of Cornell University Medical College, first as an Assistant and then Associate Professor of Surgery, and Associate Professor of Cell Biology and Anatomy. He received his Ph.D. in experimental medicine from the Medical Faculty at the University of Gothenburg, Gothenburg, Sweden, in 1986. His research interests have focused on the pathophysiologic role of cytokines in the host response to acute and chronic inflammation.

Dr. Moldawer currently lists 261 peer-reviewed publications. He has received independent funding from the National Institutes of Health continuously since 1988. During this period, Dr. Moldawer has pursued research into the role that dysregulation between proinflammatory cytokine and cytokine inhibitor production plays in the pathologic host response to acute inflammatory processes, such as sepsis and systemic inflammatory response syndromes, and to chronic inflammatory processes, such as cancer and AIDS-associated cachexia. In 1998 Dr. Moldawer received the Merit Award from the National Institute of General Medical Sciences, extending his current NIH support through the year 2006. Dr. Moldawer is also co-Director of the Protein Analysis and Cell Biology Core, and a member of the Steering Committee, of a National Institute of General Medical Sciences Large Scale Collaborative Research Program (Glue Grant) entitled "Inflammation and the Host Response to Injury," funded through 2006 to introduce functional genomics and high throughput proteomics into trauma and sepsis research.

In the teaching arena, Dr. Moldawer is the principal investigator on a training grant from NIH to provide surgical residents in training with a two-year research stint in molecular biology and gene therapy. He is one of only a small number of Ph.D.'s in the country who holds the academic rank of Full Professor in a department of surgery. Since 1988, Dr. Moldawer has trained 31 surgical residents in research methodologies (19 at the University of Florida). Sixteen of these surgical residents have continued in academic training programs, and eight are currently on the faculty of colleges of medicine.

Dr. Moldawer has sat on or currently sits on the editorial board of five journals, including: *the American Journal of Physiology, Journal of Parenteral and Enteral Nutrition, Surgical Infections*, and *Shock*. He is an Associate Editor of Shock and the *American Journal of Physiology*, as well as Section Editor of *Current Opinion in Clinical Nutrition and Metabolic Care*. He is a past member of the Metabolic Pathology Study Section of NIH; a current ad hoc member of the Surgery, Anesthesiology, and Trauma Study Section; and serves in special initial review groups for the National Institute of General Medical Sciences in the fields of graduate medical education and burn and trauma physiology.

LISA D. BROOKS, PH [

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ROBERT A. STAR, MD

VIVIAN OTA WANG, PH D

HECTOR R. WONG, MD

Patricia E. Molina, MD, PhD

Professor of Physiology Louisiana State University Health Sciences Center New Orleans, Louisiana

Speaker Topic: Neurobiology of the Stress Response; Neuroendocrine-Immune Interactions

In addition to her professorship, Dr. Molina is the Director of Education for the Alcohol Research Center at LSUHSC. She received her M.D. from the Universidad Francisco Marroquín in Guatemala and her Ph.D. in Physiology from LSU Medical Center, New Orleans. Her research focuses on understanding the neuroendocrine and opiate mechanisms involved in modulation of hemodynamic, metabolic, and inflammatory responses to shock and trauma. Studies in her laboratory use conscious unrestrained rodents to investigate the compensatory mechanisms that are affected by stress, alcohol intoxication, and analgesic use during the period prior to or immediately following traumatic injury. Dr. Molina is particularly interested in understanding how host defense mechanisms are affected by the deranged neuroendocrine response to tissue injury and acute hemorrhagic shock.



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VIVIAN OTA WANG, PH D

HECTOR R. WONG, MD

Gerald M. Saidel, PhD

Professor, Department of Biomedical Engineering Director, Center for Modeling Integrated Metabolic Systems Case Western Reserve University Cleveland, Ohio

Speaker Topic: Dynamic Systems Modeling of Cellular Metabolic Processes to Predict Organ and Whole-Body Responses

Dr. Saidel received his Ph.D. from The Johns Hopkins University. He is a member and former President of the Biomedical Engineering Society. He is also a founding member of the American Institute of Medical and Biological Engineers. Dr. Saidel has authored more than 120 research articles in peer-reviewed journals.

Dr. Saidel's major research interests include mass and heat transport and metabolism in cells, tissues, and organ systems. His major teaching activities emphasize mathematical modeling and analysis of biomedical systems, transport processes, and chemical reactions; and optimal parameter estimation and experiment design. Also, Dr. Saidel has served as Research Advisor for 22 M.S. and 22 Ph.D. students at Case Western Reserve University.



JEFFREY R. BOTKIN, MD, MPI

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VIVIAN OTA WANG, PH D

HECTOR R. WONG, MD

Adam Seiver, MD, PhD

Vice President, Clinical Affairs Chief Medical Officer Respironics, Inc.-Hospital Division Los Altos Hills, California

Speaker Topic: Cardiac Output Variations: Modeling Controller Dysfunction

Dr. Seiver serves as VP, Clinical Affairs, and Chief Medical Officer for the Hospital Division of Respironics, Inc., where he provides medical direction to Marketing and R&D. He holds appointments as Adjunct Clinical Associate Professor of Surgery and Consulting Associate Professor of Engineering at Stanford University. He has practiced surgical intensive care and trauma surgery for 20 years, with research focused on applications of mathematics and engineering to critical care. He holds an M.D. and Ph.D. from Stanford University, an M.B.A. from Duke University, and a fellowship in the American College of Surgery and the American College of Critical Care Medicine.

ROBERT A. STAR, MD

Robert A. Star, MD

Chief, Renal Diagnostics and Therapeutics Unit Senior Scientific Advisor Senior Advisor for Clinical Research National Institute of Diabetes and Digestive and Kidney Diseases National Institutes of Health Bethesda, Maryland

Speaker Topic: The NIH Roadmap: Re-Engineering the Clinical Research Enterprise

Dr. Star currently holds the following professional positions: Chief of the Renal Diagnostics and Therapeutics Unit, NIDDK; Senior Investigator, NIDDK, NIH; Senior Scientific Advisor, Translational Biology, NIDDK, NIH; Senior Advisor for Clinical Research, Office of Science Policy and Planning, Office of the Director, NIH; and Clinical Professor, George Washington University. He has worked on the clinical research portion of the NIH Roadmap, and coordinates the Trans-NIH Clinical Research Workforce Committee.

Dr. Star received his B.A. from Harvard College and his M.D. from Harvard Medical School and MIT Joint Program in Health Sciences and Technology. He was awarded the Young Investigator Award from the American Society of Nephrology and American Heart Association

Dr. Star's laboratory studies acute renal failure and sepsis and has developed a clinically relevant model of sepsis-induced acute renal failure and several MRI imaging methods. Dr. Star frequently lectures at scientific meetings on acute renal failure and sepsis. He is widely published, with numerous articles and book chapters.











FRANK STÜBER, MD

Frank Stüber, MD

Director of Operating Room and Vice Chair Department of Anesthesiology and Intensive Care Medicine, Bonn University Bonn, Germany

Speaker Topic: Genomic Polymorphisms and Outcome in Patients with Severe Sepsis

Since March 2002 Dr. Stüber has been Director of the OR and Vice Chair of the Department of Anesthesiology and Intensive Care Medicine at Bonn University. He received his M.D. from Christian-Albrechts-University Kiel and is board-certified in anesthesiology with a subspecialty in intensive care medicine.













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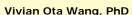
HECTOR R. WONG, MD











Program Director Ethical, Legal, and Social Implications Program National Human Genome Research Institute National Institutes of Health Bethesda, Maryland

Vivian Ota Wang is a Program Director of the Ethical, Legal, and Social Implications Program of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health. She is responsible for the complex traits, behavioral and community research portfolio.

Prior to joining NHGRI, she held faculty positions at Rutgers, Arizona State, and Vanderbilt Universities where she maintained a research program focused on race and racial attitudes related to genetics research, clinical issues, and education. Her work has been published in genetics, counseling, and psychology venues. She has been on the editorial boards of the *Journal of Genetic Counseling* and the *Journal of Multicultural Counseling and Development*.

Dr. Ota Wang has served on national committees including the: Ethical, Legal, and Social Issues (ELSI) Research Advisory Group; International Haplotype Map Project Steering Committee and ELSI Group (NIH-National Human Genome Research Institute), and the Cancer Genetics Network Behavioral Sciences Research Advisory Board (NIH-National Cancer Institute). She was on theBoard of Directors and Executive Committee of The Genetic Alliance and was a member of the Minority Women's Health Panel of Experts (DHHS-Office on Women's Health) where she was Chair of the Policy/Implementation Subcommittee. Internationally, she was active in United Nations Educational, Scientific, and Cultural Organization's (UNESCO) Asia-Pacific Regional education initiatives.

Dr. Ota Wang received a BA from Colorado College, an MS in Genetic Counseling from the University of Colorado and an MPhil and PhD in Psychology from Columbia University. She is a Fellow of the American College of Medical Genetics, and a Diplomate of the American Board of Genetic Counseling, and a Clinical Laboratory Specialist in Cytogenetics CLSP(CG).

HECTOR R. WONG, MD

Hector R. Wong, MD

Associate Professor of Pediatrics Director, Division of Critical Care Medicine Cincinnati Children's Hospital Medical Center University of Cincinnati College of Medicine Cincinnati, Ohio

Speaker Topic: Microarray Analyses in Pediatric Septic Shock

Dr. Wong trained in pediatrics and in the subspecialty of pediatric critical care medicine, and combines clinical practice in the pediatric intensive care unit with an active research effort. His work in basic science involves heat shock protein-related biology. He is also involved in the area of genomics and pediatric septic shock. This project is a multi-institutional effort to develop a national-level genomic database of children with SIRS and septic shock. The data base is currently being mined to elucidate the genome-level expression patterns that define these clinical entities.















HOTEL

GETTING TO BETHESDA

Accommodations for Symposium attendees are available at several hotels in the Bethesda area for the nights of April 20 - 22, 2005. You are encouraged to make your hotel reservation as soon as possible to obtain any special rates. Reservations are based on availability.

All hotels are located less than 2 miles from the National Institutes of Health, and a few are blocks from the NIH campus.

Four Points Sheraton (.30 miles from NIH) 8400 Wisconsin Avenue www.fourpoints.com

\$153.00 cutoff date: March 21, 2005 301-654-1000 1-800-325-3535

American Inn of Bethesda (.40 miles from NIH)

8130 Wisconsin Avenue www.american-inn.com \$99.00-\$129.00 (ask for the conference rate) 301-656-9300 1-800-323-7081

Holiday Inn Select of Bethesda (.40 miles from NIH)

8120 Wisconsin Avenue www.holiday-inn.com/bethesdamd \$153.00 (ask for the conference rate) 301-652-2000 1-877-888-3001

Bethesda Marriot Hotel (1.58 miles from NIH)

5151 Pooks Hill Road www.marriott.com \$249.00 (the prevailing rate) 301-897-9400 1-800-228-9290

Bethesda

www.thedistrict.com

More than 200 of the finest restaurants and shops are within walking distance of the hotels. The following websites will update you on local activities. www.bethesda.org



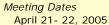


HOMELAND SECURIT









Meeting Times

Thursday, April 21, 8:00 a.m. - 4:30 p.m. Friday, April 22, 8:00 a.m. - 4:00 p.m.

Meeting Location

William H. Natcher Conference Center National Institutes of Health 45 Center Drive Bethesda, MD 20814 301-496-9966

The Natcher Conference Center is part of the National Institutes of Health (NIH) and is located in the Natcher Building, 45 Center Drive, on the NIH campus in Bethesda, Maryland. The Symposium will be held in the Auditorium, located on the lower level of conference center.

Visitor parking is very limited; we encourage Symposium participants to use public transportation. The Conference Center is a short walk from the Medical Center Metrorail Station on the Red Line. If you must drive, limited parking may be available near the Natcher Conference Center.

Messages can be left for symposium participants between the hours of 8:00 a.m. and 5:00 p.m. by calling 301-496-9966 extension 211. Faxes can be sent to 301-480-5982.

GETTING TO BETHESDA

BY AIR
BY TRAIN
SUBWAY TO NIH
AIRPORT SHUTTLE
DRIVING TO NIH
PARKING

HOMELAND SECURITY

By Air

The greater Washington area, including Bethesda, is served by three major airports: Ronald Reagan National, Washington-Dulles International, and Baltimore-Washington International. Travel time from all three airports to the Bethesda-area hotels and the NIH campus is approximately 45 minutes to 1hour. For more details: www.mwaa.com and <a href="w

By Train

Union Station serves the greater Washington area. It is approximately 45 minutes to Bethesda-area hotels and the NIH campus from the station. For more details: www.unionstationdc.com

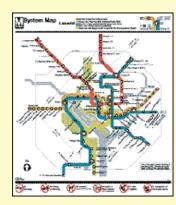
Subway to NIH

Take the Red Line toward Shady Grove or Grosvenor. Exit at the Medical Center Metro Station. At the top of the escalators, take the stairs or ramp to your left and follow the path to the Natcher Conference Center. For more METRO information, please visit www.wmata.com

The subway is available from Ronald Reagan National Airport and Union Station.

Ronald Reagan National Airport:

From airport Terminals B and C, take the pedestrian bridge to Metrorail's Reagan National Airport Station located on the Yellow and Blue Lines. Take a Yellow Line train to Gallery Place or take a Blue Line train to Metro Center and transfer to the Red Line. On the Red Line, take a train toward Shady Grove or Grosvenor to the Medical Center Station.



Union Station:

Union Station is located on the Red Line. Take a train toward Shady Grove or Grosvenor to the Medical Center Station.

Taxi to NIH

From Ronald Reagan National Airport:

12 miles from NIH one way fare is approximately \$40.

From Dulles International Airport:

26.2 miles from NIH; one-way fare is approximately \$50.

From Baltimore-Washington Airport:

34.5 miles from NIH; one-way fare is approximately \$70.

Airport Shuttle to NIH or Hotel

In most cases, airport shuttles will cost less than a taxi. Several shuttle services, including the two listed below, operate to

and from the local airports. You may visit the websites or call prior to travel to make necessary arrangements. When making reservations, please be prepared with the following information: airline, flight number, and expected time of arrival.

SuperShuttle Transportation www.supershuttle.com 1-800-258-3826

BWI Airport Shuttle www.theairportshuttle.com 1-800-776-0323

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Driving to NIH

For more detailed driving directions

From Points North

- -Take I-95 south toward Washington, DC. At I-495 (Capital Beltway), head west toward Silver Spring/Bethesda.
- -Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda.
- -At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Points South

- -Take I-95 north toward Washington, DC. At I-495 (Capital Beltway), head north toward Silver Spring/Bethesda.
- -Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda.
- -At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Ronald Reagan National Airport

- -Head North on the George Washington Parkway for approximately 5 miles.
- -Exit onto I-495 (Capital Beltway), heading north to Maryland.
- -Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head South toward Washington/Bethesda.
- -At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

From Baltimore-Washington International Airport

- -Take the Baltimore-Washington Parkway south toward Washington, DC. At I-495 (Capital Beltway), head west toward Silver Spring/Bethesda.
- -Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda.
- -At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

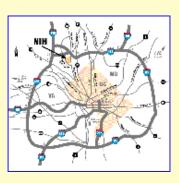
From Dulles International Airport

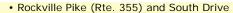
- -Head east on the Dulles Airport Access Road for approximately 13 miles.
- -Exit onto I-495 (Capital Beltway), heading north to Bethesda/Baltimore.
- -Exit 34, which is Rt. 355 (Wisconsin Ave./Rockville Pike) and head south toward Washington/Bethesda.
- -At the fourth traffic light, turn right onto South Drive and bear right to the vehicle inspection area.

For more detailed driving directions

Entrances and Exits

All visitors must use the following two entrances:





Old Georgetown Road and Center Drive

All visitor vehicles, including taxicabs and hotel and airport shuttles, will be inspected beforebeing allowed on campus. Visitors will be asked to show a photo ID and state the purpose of their visit. Be sure to allow extra time for this procedure.

Parking

Parking on the NIH campus is extremely limited. There is a small paid parking lot next to the Natcher Conference Center. The parking fee is \$2 per hour for the first three hours or \$12 per day. For more details: parking.nih.gov/parkinglots.cfm.



Entrances, Exits and Parking Map



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GETTING TO BETHESDA

HOMELAND SECURITY MEASURES









National Institutes of Health

To enter the NIH campus, all visitors must present one government-issued photo ID (i.e., Federal employee badge, driver's license, passport, green card, etc.). Visitor vehicles will be inspected at the campus perimeter.

Natcher Conference Center

All nonfederal employees will need to pass through Security. Plan to have two forms of identification including one with a picture. Visitors may be required to pass through a metal detector and may have their bags, backpacks, or purses inspected or x-rayed as they enter Natcher Conference Center. Meeting participants may want to leave extra bags or personal items at their hotel to minimize the time needed for inspection.

Please allow for an additional 20 minutes to pass through Natcher Conference Center Security.

International Travelers

At this time, the US Department of Homeland Security has a high-tech registration system in place, to fingerprint and photograph foreign visitors who are required to have visas as they enter through designated US airports and seaports. Visitors with visas will be photographed and have their index fingers electronically fingerprinted or verified upon entering or exiting the US. The program will exempt permanent US residents and foreign visitors from 27 countries who do not need visas to enter the US.

Currently, 27 countries participate in the Visa Waiver Program: Andorra, Australia, Belgium, Brunei, Denmark, Finland, France, Germany, Iceland, Ireland, Italy, Japan, Liechtenstein, Luxembourg, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom.

To learn more information about the visa requirements for traveling to the US, please check out the Travel and Transportation information at www.dhs.gov/us-visit.

Overview Agenda Speakers Hotel & Travel Registration Abstracts Exhibitors Contacts

REGISTRATION INFORMATION

ON-LINE REGISTRATION

Registration provides access to all sessions, and breaks mentioned in the agenda and access to the Technical Exhibit Hall, Poster Session and Poster Reception.

Registration Fee:

General - \$125
Federal Employee - no fee
In Training - no fee
Submitting Abstract - no fee

ON-LINE REGISTRATION IS NOW CLOSED.

You are welcome to register at the symposium. A suggestion: kindly bring your business card to speed up your on site registration

Boxed Lunch:

You may order a boxed lunch for \$15.00. The lunch will include a choice of tuna salad, grilled chicken or roasted vegetable sandwich; chips, apple, cookie, and a beverage. These lunches will be available in the private dining rooms of the Natcher Conference Center Café. Please make arrangements for payment prior to the conference.

Payment Methods:

Payment for registration and boxed lunch(es) may be made with personal or business check, money order or credit card (American Express, MasterCard or Visa).

Confirmations:

Confirmation of Symposium registration will be sent via email.

Receipts:

Receipts for Symposium registration fee and lunch will be sent via email.

Substitutions:

Prior to the Symposium you may request a substitution. Please send in notice of cancellation and request to substitute. We will accept substitutions until Friday, April 8, 2005.

Cancellations/Refunds:

Written requests for cancellation must be received by April 8, 2005. Refunds will be made less a \$25 processing fee.



REGISTRATION INFORMATION

ON-LINE REGISTRATION

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You are welcome to register at the symposium.

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The symposium Organizing Committee invites you to submit an abstract of your scientific research to be considered for presentation during the Symposium poster session. Several posters will be selected for oral presentation and two abstracts will receive Science Awards(\$500 each). The deadline for submission is March 1, 2005. Notice of acceptance will be sent to authors by March 22, 2005.

Guidelines for Preparation and Formatting

Abstracts should be single-spaced and contain a maximum of 300 words. They must be a single-spaced WordPerfect or Word document, using 12-point Times New Roman or similar font.

Abstracts should include the following information:

Title: Uppercase letters

Names and affiliation of authors: Name of presenter underlined, and affiliation of authors.

Example of preferred author/affiliation format:

John Doe¹, Mary Smith², Peter Jones ³.

¹National Institute of General Medical Sciences, ²Channing Laboratory, Harvard University, and ³University of California, San Francisco.

Abstract text: The abstract should have four clearly identifiable components: Background, Methods, Results, and Conclusion. You may use special Greek or mathematical characters in your abstract as well as charts and images. Text, charts, and images of your abstract must fit within a 5-inch by 5-inch block.

Source of funding: List primary and secondary sources.

Financial disclosure: Authors of scientific oral or poster presentations who have entered into a financial relationship with sponsoring companies or organizations about whose product or services they are reporting must include a disclosure statement at the end of their abstracts, e.g., "Research supported by ACME Pharmaceuticals." It is recognized that much scientific research is supported by organizations that have a commercial interest in the results of the research. The disclosure policy is not intended to discourage such support or restrict the dissemination of the research, but rather to permit members of the audience to form their own judgments about the research with the full disclosure of the facts.

Contact information: Please include the following: your name, position, department, affiliation, mailing address, telephone, and fax numbers.

Guidelines for Submission

Please submit your abstract as an e-mail attachment to Nicole@strategicresults.com by March 1, 2005. In the subject line put "Abstract for FG Symposium." A confirmation reply will be sent to you.

If you have any problems with e-mail submission, please contact Nicole Mitchell at 410-377-0110.







Exhibition date: April 21, 2005 all day

Symposium dates: April 21- 22, 2005

Location: Atrium Level

Natcher Conference Center National Institutes of Health

Bethesda, Maryland

Exhibit fee: \$695

Exhibitor Prospectus: Click here to receive the prospectus

Exhibitor Information: Sue Dilli

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Thank you!









Jeffrey R. Botkin, MD, MPH

Professor, Department of Pediatrics; Adjunct Professor of Human Genetics Adjunct Professor, Department of Internal Medicine - Division of Medical Ethics University of Utah School of Medicine Salt Lake City, Utah

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"Genetic Determinism and Genetic Exceptionalism"

Genetic exceptionalism is the concept that genetic information is qualitatively different than other forms of medical information. The implication of genetic exceptionalism is that genetic research requires a heightened level of scrutiny compared to many other types of biomedical research. This presentation outlines ways in which genetics poses important challenges for the conduct of research. These challenges are not unique to genetics. Characteristics that justify increased scrutiny for genetic and non-genetic protocols include potential impacts on others such as family members, risks for stigma or discrimination, predictive power for future illness, and the psychological impact of predictive information. A brief history of the social status of genetic information also will be presented.

Jeffrey R. Botkin, MD, MPH

Program Director Genetic Variation Program National Human Genome Research Institute National Institutes of Health Bethesda, Maryland

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"The International HapMap Project"

The International HapMap Consortium is developing the human haplotype map, which will be a resource for studies relating genetic variation to health and disease. The map is being developed with 270 samples, from Yoruba in Ibadan, Nigeria, Japanese from Tokyo, Han Chinese from Beijing, and CEPH from Utah (residents with ancestry from northern and western Europe). The map of SNPs at 5 kb or closer spacing has recently been completed, with about 1 million SNPs. The full map with about 5 million SNPs will be completed in October of 2005. Other SNPs, including functional SNPs, are expected to have a high likelihood of being strongly associated with SNPs in this map. The HapMap will allow association studies to genotype a subset of SNPs that cover regions of interest or the entire genome comprehensively and efficiently. (www.hapmap. org)

Lisa D. Brooks, PhD









Harry Edison
Professor, Surgery
Division of General
Surgery
Chief; Burn, Trauma,
Surgical Critical Care
Section
Washington
University School of
Medicine in St. Louis
St. Louis, Missouri

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"Genetic Testing in the Acute Care Environment: Ethical, Legal and Social Aspects"

Family histories have long suggested an heritable predisposition to acute illnesses, including myocardial infarction, stroke, arrhythmia and infection. Family histories have also suggested heritable susceptibilities and adverse effects in response to medications used to treat acute illnesses. Recent studies suggest that certain genetic variations ("alleles") can be associated with these heritable susceptibilities, creating a potential to modify prognosis, diagnosis, and treatment of serious illnesses based on genetic testing. The usual setting in which counseling for genetic testing takes places over many encounters to ensure that the patient/subject is adequately informed about the indications, risks, benefits and alternatives to such testing. In the acute care setting, there are a time imperative, often a surrogate decision-maker, and multiple complex health issues. Yet there are concerns among patients and surrogates regarding potential for employment discrimination, insurance (disability, health and life) discrimination, and reimbursement for such testing. This presentation will examine the potential for discrimination associated with genetic testing in the acute care environment; confront the issue of consent in the acute circumstance; and consider the issues of linking archived specimens with clinical outcome.

Timothy G. Buchman, PhD, MD









Trinad Chakraborty, PhD

Professor of Microbiology
Director of the Institute of
Medical Microbiology
University Teaching
Hospital of Giessen
Giessen, Germany

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"Genome-Wide Molecular Signatures in Sepsis"

Introduction

Trauma is a major source of morbidity and mortality. Severely injured patients who survive the early posttraumatic period are confronted with substantial alterations in immune function. This systemic inflammatory response syndrome (SIRS) involves activation and suppression of both the innate and adaptive immune responses. These perturbations in immune function often contribute to sepsis and posttraumatic organ failure syndromes. In this setting, circulating immune cells play a pivotal role in the development of sepsis and posttraumatic multiple organ dysfunction syndrome (MODS). Therefore, a broad analysis of the responses by peripheral blood cells to severe traumatic injury might permit a better understanding of the early pathophysiological sequences in patients at risk of MODS leading to an unfavorable outcome. We used oligonucleotide arrays to assay the complexity and diversity of the inflammatory response to a defined traumatic injury at the level of the human transcriptome in peripheral blood.

Aims

In this study, we aim at uncovering the biological reasons why patients can have dramatically different outcomes after suffering similar traumatic insults, and seek a genome-wide view of the regulatory events in response to septic challenge in high-risk patients, including those with multiple trauma, severe pneumonia, or newborn respiratory distress syndrome. The specific aims of the current study were i) to explore the early genome-wide changes in gene expression of these patients, ii) to determine whether patterns of gene expression were associated with a differential clinical outcome in this patient population and iii) to identify candidate genes for susceptibility to sepsis and use them for high throughput SNP-screening.

Results and Conclusions

A total of more than 800 RNA-samples were obtained from patients with multiple trauma, severe pneumonia and preterm infants.

A sequential mRNA array screening analysis of ~ 10 000 genes from peripheral blood of patients with multiple trauma was performed during the complete posttraumatic phase (14 days) in order to identify potential trauma-sensitive patterns of gene expression. The findings clearly demonstrate microarrays enable effective screening of mRNA expression alterations induced by trauma in peripheral blood. Depending on the clinical outcome (non-sepsis/sepsis) of the patients, ~700 genes differ significantly at the time point of admission to the ICU in those patients who developed sepsis. Consequently, the expression of these genes might be suitable as classifiers of patient outcome. Further analysis of the putative biological function of the identified genes revealed a regulatory network of inflammatory- and stress- responses, apoptosis and development. These data are consistent with the hypothesis that peripheral blood expression profiles can be used as molecular tools to aid diagnosis and prognosis after critical injury.

H. Hossain*, S. Little+, S. Tchatalbachev*, T. Menges+, G. Hempelmann+, T. Chakraborty*

- * Department of Medical Microbiology; University of Giessen;
- + Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy,

University of Giessen



Samir M. Hanash, MD, PhD

Full Member Fred Hutchinson Cancer Research Center Seattle, Washington

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"Proteomic Global Profiling for Cancer Biomarker Discovery"

There is substantial interest in applying proteomics to biomarker discovery. Proteomics is particularly suited for profiling biological fluids and uncovering circulating markers and profiling disease tissue to identify dysregulated pathways that may be targets for individualized therapy. Proteomic approaches currently implemented include direct profiling of serum and tissue using mass spectrometry, sample pre-fractionation prior to mass spectrometry to capture sub-proteomes rich in diagnostic markers, and the use of protein microarrays. However, a framework for biomarker discovery has yet to emerge. There is also a substantial need for resources such as standardized tissues and affinity capture agents to facilitate discovery and validation. An organized effort to develop resources for biomarker discovery will be of substantial benefit to the field. The current status of such effort will be reviewed.

Samir M. Hanash, MD, PhD









Jean-Paul Mira, MD, PhD Professor of Medical Intensive Care Cochin-St.Vincent de Paul University Hospital Medical Intensive

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Care Unit

Paris, France

"Pathogen Recognition Receptors Polymorphism"

Innate immunity represents the firstline host defense necessary to limit infection in the first hours after pathogen invasion. Immediate protection against microorganisms involves three mechanisms: recognition of the pathogen, phagocytosis and elimination of invading pathogens, and development of an inflammatory response necessary to the resolution of the infection. Throughout evolution, innate immunity has developed a very efficient system that recognizes invariant molecular constituents of the infectious agents called PAMPs (Pathogen-Associated Molecular Patterns). This system of detection is currently referred to as Pattern Recognition Receptors (PPRs) and can be divided into the following three classes: soluble receptors that are plasma proteins, such as the mannose binding lectin (MBL) and the components of the complement system; endocytic receptors, such as the Fc_ receptors and the mannose receptors; and signaling receptors, such as the Toll-Like Receptors (TLRs) and CD14. During the last five years, polymorphic genes of the pathogen recognition receptors have been intensively investigated and associated with an increased susceptibility and/or mortality of severe sepsis and septic shock primarily through inefficient clearance of pathogens.

MBL is a member of the collectin family of proteins. This calcium-dependent plasma lectin binds to sugars and possibly endotoxin on all microbial surfaces and then activates complement, acting as a so-called ante-antibody. Moreover, MBL can directly act as an opsonin and bind to specific receptors expressed on the cell surface of various cell types, including monocytes. Thus, MBL clearly seems to be a pluripotent molecule of the innate immune system. The concentrations of MBL in human plasma are genetically determined and are profoundly reduced by either structural gene mutations or by promoter gene polymorphisms. Many case reports and these three large series indicated that structural variants in the MBL gene, which result in decreased MBL plasma levels, are associated with susceptibility to a range of infections in adults and

children such as severe pneumococcia or letal meningococcemia.

Fc_ receptors on the phagocytic cell surface bind the Fc region of IgG antibody and mediate binding, phagocytosis, and destruction of bacteria opsonized with IgG. Among this class of receptors, Fc_RIIa (CD32) is a low-affinity receptor that interacts only with complexed IgG and is the sole Fc_R class that can bind IgG2. Human IgG2 antibodies play a crucial role in immune defense against sepsis attributable to encapsulated bacteria (Streptococcus pneumoniae, Hemophilus influenzae, and Neisseria meningitidis). It has been clearly demonstrated that selective IgG2 subclass deficiency may result in recurrent upper and lower respiratory tract infection attributable to encapsulated bacteria. A frequent point mutation within the Fc_RIIa gene seems to be linked to bacteremic pneumococcal pneumonia and higher susceptibility to severe meningococcal disease.

Toll-Like receptors (TLRs) play an important role in innate immunity from insects to mammals. The TLR family consists of cell surface and endosomal receptors that recognize specific, conserved specific PAMPs present on infectious agents. Stimulated TLRs activate the transcription factor nuclear factor _B and a signaling cascade that culminates in the increased expression of immune and proinflammatory genes, and it thereby plays an essential role in innate and adaptive immunity. Several Single Nucleotide Polymorphisms (SNPs) within TLRs genes appear to result in an altered innate immune response:

- TLR4 is crucial to endotoxin detection and initiation of many of the responses observed in sepsis. The TLR4 locus contains two missense SNPs, which confer alterations in the extracellular domain of the receptor and have been found to positively correlated with gram-negative infections and septic shock in ICU patients. However, these SNPs may have beneficial effects, as they seem to protect from atherosclerosis and related diseases.
- TLR5 recognizes bacterial flagellin and its gene have a point mutation that introduces a stop codon within the ligand binding domain (TLR5392STOP). The TLR5392STOP mutation functions as a dominant negative receptor that severely impairs signaling and has been associated with susceptibility to pneumonia caused by the flagellated bacterium Legionella pneumophila.
- TLR2 plays a central role in the innate immune response to a wide variety of Gram positive bacteria. In Human, Tlr2 gene is located on chromosome 4 and contains a large number of polymorphisms both in the non coding and coding sequences. Among all these genetic variants, two polymorphisms (Arg677Trp and Arg753Gln), which attenuate receptor signalling, enhance the risk of acute severe infections (Gram positive septic shock), tuberculosis and leprosy in

different populations.

The increasing understanding of molecular medicine will shift clinical practice from empirical treatment to therapy based on a molecular mechanism of infectious diseases. As genetic screening to evaluate the individual risk factors for infectious disease will come to place, it may be predicted that knowledge of the role alteration or lack of PRR function play in the pathogenesis of infectious diseases could contribute to the design of new therapeutic strategies, including prevention, pharmacological intervention and vaccine development.

Jean-Paul Mira, MD, PhD









Patricia E. Molina, MD, PhD

Professor of Physiology Louisiana State University Health Sciences Center New Orleans, Louisiana

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"Neurobiology of the Stress Response; Neuroendocrine-Immune Interactions"

Acute injury immediate activates neuroendocrine mechanisms aimed at restoring hemodynamic and metabolic counterregulatory responses. These counterregulatory responses are mediated by the systemic and tissue localized release of neuroendocrine signaling molecules known to affect immune function. This has led to the recognition of the importance of neuroendocrine-immune modulation during acute injury and throughout the recovery period. The neuroendocrine mechanisms involved in restoring homeostasis play important roles in mediating acute counterregulatory stress responses to injury.

In addition to their recognized cardiovascular, hemodynamic and metabolic effects, neuroendocrine mediators released in the periphery modulate immune function through receptor specific pathways. In turn, cytokines, chemokines and neuropeptides released by the immune system influence peripheral and central neurotransmission leading to the conceptualization of a bidirectional neuroimmune communication system. The reflex activation of this bidirectional neuroimmune pathway in response to injury, integrated with the parasympathetic nervous system, opioid and glucocorticoid pathways responsible for orchestrating the counterregulatory stress response, results in dynamic regulation of host defense mechanisms vital for immune competence and tissue repair. This presentation will provide the biological framework for the integration of our understanding of the neuroendocrine mechanisms involved in mediating the stress response and their role in neuroimmunomodulation during and following traumatic injury.

Patricia Molina, MD, PhD

Gerald M. Saidel, PhD

Professor,
Department of
Biomedical
Engineering
Director, Center for
Modeling Integrated
Metabolic Systems
Case Western
Reserve University
Cleveland, Ohio

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"Dynamic Systems Modeling of Cellular Metabolic Processes to Predict Organ and Whole-Body Responses: Potent 35.595ipnP < tiono PrCrital



* Supported by a grant (P50- GM66309) from the National Institutes of General Medical Sciences (NIH)

Gerald M. Saidel, PhD

Adam Seiver, MD, PhD

Vice President, Clinical Affairs Chief Medical Officer Respironics, Inc.-Hospital Division Los Altos Hills, California

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"Cardiac Output Variations: Modeling Controller Dysfunction"

Computer-based analysis of dynamic patterns in physiological signals may give new insights into organ responses in critical illness. Healthy physiological systems exhibit irregular variability while diseased systems display increased signal regularity. We discovered peculiar, ultra low-frequency periodic sinusoidal oscillations in cardiac output (ULF-CO) in data collected from critically ill surgical and trauma patients. Ten patients with sepsis or the systemic inflammatory response syndrome exhibited 18 episodes of ULF-CO with frequencies ranging from 0.0028 to 0.000053 Hz (periods, 6 to 316 min). Intensive care unit mortality rate was 50%. A mathematical model of cardiac output control captures many features of these oscillations and suggests that the ULF-CO represent de-complexification of neural and humoral elements of the cardiac control system. Functional genomics may illuminate--and be illuminated by--this potential marker of organ and organ system dysfunction.

Adam Seiver, MD, PhD









Frank Stüber, MD

Director of Operating Room and Vice Chair Department of Anesthesiology and Intensive Care Medicine, Bonn University Bonn, Germany

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"Genomic Polymorphisms and Outcome in Patients with Severe Sepsis"

Background: Sepsis and its sequelae has major impact on morbidity and mortality as well as health care resource utilisation in intensive care units. Recent data of epidemiologic surveys suggest that diagnostic and therapeutic efforts to confine sepsis related adverse outcomes have not yet improved patients' course. Some ten years ago, genetic studies in intensive care patients started to provide data on genetic predisposition for incidence and outcome of severe sepsis. Genetic predisposition will be part of the "under construction" PIRO concept adopted by the surviving sepsis campaign and other international and national initiatives to fight sepsis. Time to wrap up and have a resume of as well as an outlook beyond the current status of genetic studies in sepsis.

Methods: Available data regarding genetic epidemiologic studies in sepsis will be reviewed and summarised.

Results: Genetic epidemiologic studies examining predisposition to sepsis have almost exclusively used a case control design to associate frequencies of polymorphic candidate genes with morbidity and mortality of sepsis patients. Candidate genes such as cytokine-, coagulation- and pattern recognition molecule genes have been chosen according to pathophysiological insights into processes determining sepsis injury. First results have demonstrated positive association of genomic candidate markers with morbidity as well as mortality of sepsis. Many of these initial findings lacked reproducibility which initiated debate on study design and biometrics. Recently published studies begin to mind gene-gene interaction and, thereby, promising results could be obtained employing the pro- and anti-inflammatory paradigm of sepsis.

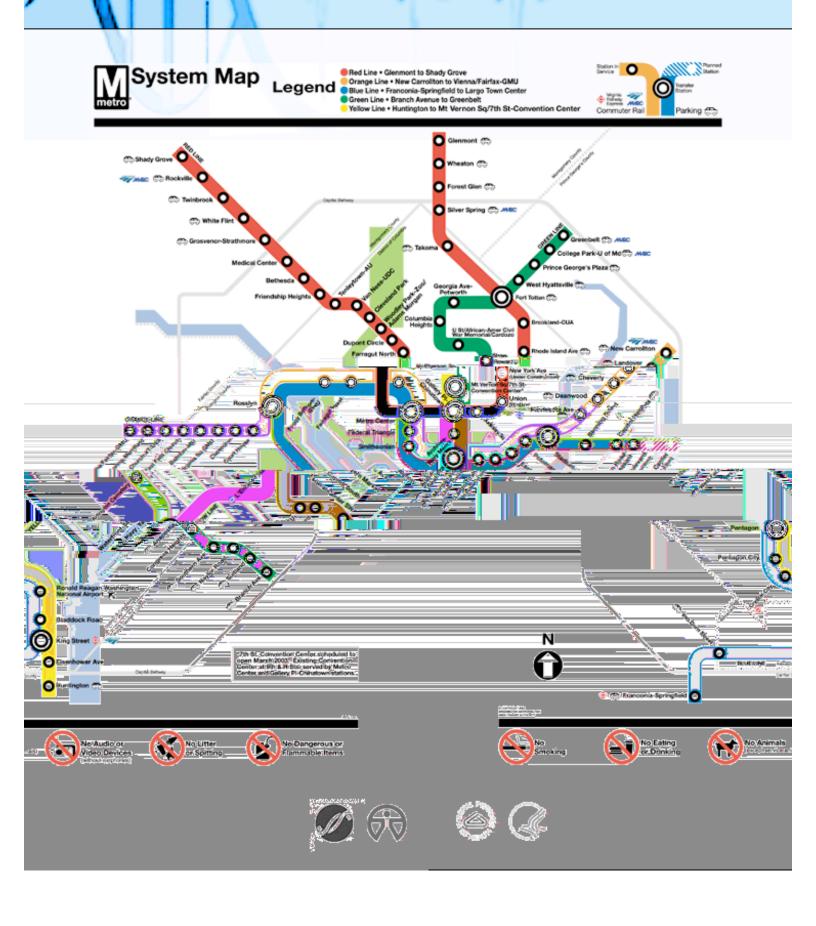
Conclusion: Currently available results do not allow definition of a generic set of genomic markers to be routinely used for risk assessment. Newly designed



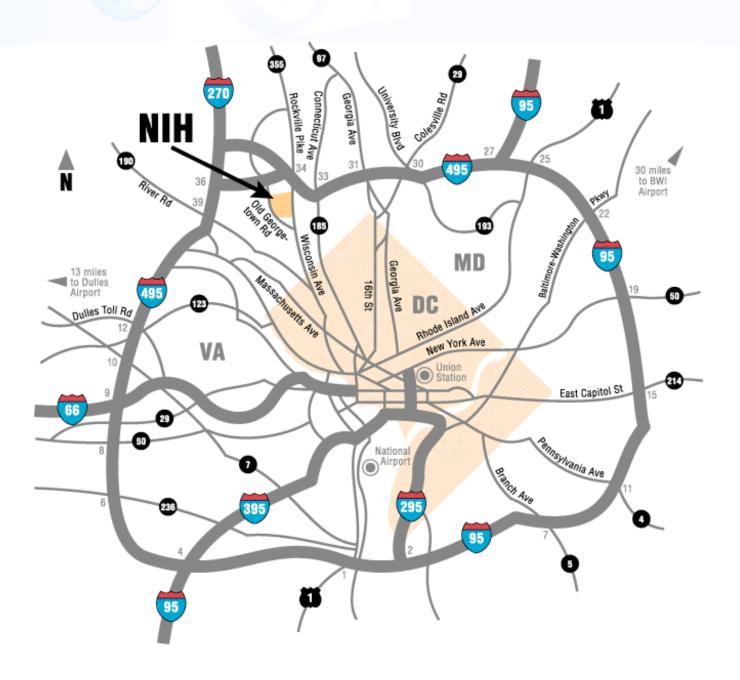
and well powered genetic epidemiologic studies have been funded and are on the way to possibly establish genomic diagnostics in order to identify risk populations and guide specific therapies in sepsis.

Frank Stüber, MD

FUNCTIONAL GENOMICS OF CRITICAL ILLNESS AND INJURY



FUNCTIONAL GENOMICS OF CRITICAL ILLNESS AND INJURY











FUNCTIONAL GENOMICS OF CRITICAL ILLNESS AND INJURY













Third Symposium on the Functional Genomics of Critical Illness and Injury

Exhibition Date: April 21, 2005

Conference Dates: April 21- 22, 2005

Natcher Conference Center National Institutes of Health Bethesda, Maryland

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AN INVITATION TO EXHIBITORS

We would like to invite you to join more than 500 participants as an *exhibitor* at the third Symposium on the Functional Genomics of Critical Illness and Injury April 21-22, 2005 at the National Institutes of Health in Bethesda, Maryland.

A wide array of influential clinicians and researchers, from specialists in intensive care to molecular biologists to biostatisticians, will be meeting once again in a unique venue to share the latest information emerging from this rapidly developing field. The 2005 meeting will focus on the rapidly evolving technologies of genomic, transcriptomic, proteomic, and metabolomic analysis and the increasing importance of computational biology, biostatistics, and systems engineering in genomic applications to critical care medicine. In addition to this topic, distinguished speakers will examine host-pathogen responses and the ethical, legal, and societal implications of genomic technologies.

As in previous years, this symposium presents a singular opportunity for exhibitors to showcase their products and services and reach a multitude of diverse disciplines. The intimate setting provided by poster sessions and presentations of oral abstracts allows participants to move about outside the plenary sessions and to view and discuss exhibits. Interest in the symposium has been high, as demonstrated by a featured report of the 2003 meeting in *JAMA* 2004;291:287, and registration for 2005 promises to exceed the numbers for previous years. This widespread appeal, combined with National Institutes of Health's commitment to support the symposia for the next five years, provides exhibitors with excellent exposure and guaranteed continuity and expansion of their audience.

We look forward to your participation at what promises to be an outstanding conference that will provide you with the opportunity to interact with leading clinical, research, and functional genomics technology professionals. Please feel free to contact me at any time to discuss the exhibit program. I can be reached at 410.377.2991 or via email at sue@strategicresults.com.

Sincerely,

Sue Dilli

A fully equipped private audio visual room is available for exhibitor presentations on a first come first serve basis.



Profile of Attendees**		
Doctors (20% Fellows)	94%	
Non-Doctors	6%	

AFFILIATION **		
Government	60%	
University/Medical School Private	21% 7%	
Hospital/Research	7%	
Military	5%	

FIELDS **		
Clinicians	37%	
Chairs/Directors/Chiefs	22%	
Research*	22%	
Professors	19%	

^{*}includes biologists, bioinformatics, engineers, biostatisticians, scientists, etc.

EXHIBITOR PACKAGE

- 5' by 2.5' covered exhibit table with chairs.
- Symposium attendee list
- Complimentary registration for two exhibitors.
- Access to all sessions, breaks, boxed lunch, and refreshments as mentioned in the conference agenda
- Listing in the Symposium Program
- Access to a fully-equipped private audio visual room is available for exhibitor presentations on a first come, first serve basis

Price

\$695 per exhibit space

Schedule

Set – up

Thursday, April 21, 2005 (7am – 8 am)

Exhibit Hall Open

Thursday, April 21, 2005 (8am – 5 pm)

See Agenda for specific exhibitor viewing times

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^{**}Profile of 2003 Attendees



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This individual signing this Contract represents and warrants that he/she is duly authorized to execute this contract on behalf of the named Exhibitor and has read and agreed to the Terms and Conditions of this Contract.		The following information is required for the exhibitor directory. Please provide a 20 – word description of the products and services you will be exhibiting. Send via email to sue@strategicresults.com , no later than April 1, 2005.
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Title:	Date:	Please print names clearly.
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TERMS AND CONDITIONS

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Set-up, show, and breakdown. Unless other wise specified Exhibitor agrees to check in and set up its display 30 minutes prior to the beginning of the event and completely remove its display from the building within 60 minutes following the completion of the event. Failure to check in by the start of the event may result in loss of space with the Exhibitor still being liable for full payment.

Fire department regulations. Exhibitors will comply with all fire and safety regulations enforced in the location of the event.

Souvenirs, premiums, samples, and prizes. Distribution of souvenirs, premiums and samples of products is permitted provided there is no interference with other exhibits. Consent to give away items, including contest prizes, will be granted by and is at the sole discretion of Strategic Results and the hosting organization. Exhibitor acknowledges that some event locations may prohibit giveaways of all kinds.

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Space requirements and restriction. One display space will include a minimum 5-foot by 2.5 -foot table, tablecloth, and **no electrical power.** The Exhibitor is to display equipment and products that will confirm to the limitations of the display space as stated above. All exhibits must be displayed within the contracted space and all Exhibitor activities must be conducted in such a way as not to infringe on the rights of other exhibitors or offend visitors to the event. Strategic Results and the hosting organization reserve the



TERMS AND CONDITIONS (cont'd)

right to reject, in whole or in part, and at any time, an exhibit which, in their sole opinions, is objectionable to exhibitors or others. No liabilities or damages whatsoever against Strategic Results and the hosting organization or any of their employees, agents, representatives, or members shall be incurred because of such rejection.

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Governing law and jurisdiction. This contract shall be governed by and subject to the laws of State of Maryland and all matters whether sounding in contract or in tort relating to the validity, construction, interpretation and enforcement of this Contract shall be determined in the circuit Court of Baltimore County, Maryland; which Court shall have exclusive jurisdiction and venue.

Damage to property. Exhibitor will not paint, tape, mail, screw, staple, drill, or tack anything to the walls, columns, floor, or ceiling of the building or adjoining displays. Exhibitor shall the be solely responsible for all damage resulting from such actions.

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QUESTIONS

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